**UNITED STATES DEPARTMENT OF COMMERCE**
**Patent and Trademark Office**
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

VB

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/215,077 | 12/18/98 | PRICE | P 23070-086711 |

HM22/1121

TOM HUNTER
C/O SKJERVEN MORRILL MACPHERSON LLP
25 METRO DRIVE
SUITE 700
SAN JOSE CA 95110

| EXAMINER | |
|---|---|
| NGUYEN, B | |
| **ART UNIT** | **PAPER NUMBER** |
| 1641 | 9 |

**DATE MAILED:** 11/21/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/215,077 | Price et al |
| **Examiner** | **Group Art Unit** |
| Bao-Thuy L. Nguyen | 1641 |

☒ Responsive to communication(s) filed on *8/8/00*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) *1-17* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) *1-8* is/are allowed.

☒ Claim(s) *9-17* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---*

## DETAILED ACTION

1. Applicant's amendment filed 8/8/00 has been received. Claims 1-17 are pending.

2. All rejections not reiterated herein below are withdrawn.

3. The text of those US codes not found in this office action may be found in a previous office action.

### *Sequence Disclosures*

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821 (a) (1) and (a) (2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice to Comply with Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is required to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821 (g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

### *Information Disclosure Statement*

5. The information disclosure statement filed 1/25/00 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information. References A35 appears to be listing of a sequence, however, no explanation as to how these sequences are relevant to the instant application. It has been placed in the application file, but the information referred to therein has not been considered.

***Response to Arguments***

**6.** Applicant's arguments with respect to references A33, A34 and A36 have been found to be persuasive, and these references have been considered. Reference A35, however, does not have any identifying information. The only information of record is an IDS listing stating that A35 is "EMHUM2 Database Accession No. HSU49835 (7/27/96) - Abstract", accompanied by a sheet of paper designated A35 with an amino acid sequence. No abstract nor any other information is available. Therefore, it cannot be determined what reference A35 is or how it is relevance.

***Claim Rejections - 35 USC § 103***

**7.** Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nyirkos et al (Biochem. J. 268:265, 1990) or Johansen et al (J. Bone Min. Res. 7(5):501, 1991) each in view of Maurer et al (Meth. Enz., 70:49, 1980) for reasons of record in paper no. 5 and is reiterated herein below.

Nyirkos et al teach the detection and quantitation of a 39 kD protein (Applicants' own publication, i.e. Johansen et al. (J. Bone Min. Res., 7(5):501, 1991), equates YKL-40 with the protein of Nyirkos et al (see page 507, column 2, lines 9-11) from synovial cells derived from the tissue of osteoarthritic and rheumatoid arthritis patients undergoing joint replacement (page 269, column 1). Nyirkos et al suggest that the protein could be useful as a marker distinguishing the synovial cell from fibroblasts. (See page 269, column 2, discussion, last paragraph).

Nyirkos et al differ from the instant invention in that they do not specifically teach the use of polyclonal or monoclonal antibodies as a means to measure YKL-40.

Johansen et al teach that a complete understanding of the physiologic function of a given cell requires knowledge of the identity and amount of each protein secreted by that cell. One of two methods to assess these proteins is an immunological assay for antigens (see page 501, Introduction). Johansen et al were able to detect and quantitate a new protein, YKL-40, from human osteosarcoma cells in SDS gels (see page 507, column 1, top).

Johansen et al differs from the instant invention in that they do not specifically teach the use of polyclonal or monoclonal antibodies as a means to measure YKL-40.

Maurer et al teach that antibodies can be prepared against virtually any macromolecule (page 50, second full paragraph), that polyclonal antibodies can be produced via immunization of a mammal (page 51, under "animal Species"), and that monoclonal antibodies can be produced from hybridomas (pages 65-67). Maurer et al further teach the many utilities of monoclonal and polyclonal antibodies, such as detection and assaying or concentrating and purifying an antigen of interest (page 49).

It would have been obvious to one of ordinary skill in the art to use either polyclonal or monoclonal antibodies in an immunoassay for YKL-40, since both Nyirkos et al and Johansen et al teach the need for detection and quantitation of the molecule and Johansen et al specifically teach that immunoassay is one of two means by which proteins produced by different cell types can be identified, and Maurer et al teach that antibodies, both polyclonal and monoclonal, can be produced against virtually any macromolecule, and can be used in an assay for its detection, providing one of ordinary skill in the art a high expectation of success in raising the necessary antibodies and motivation for use of the antibodies in an assay.

**8.** Claims 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nyirkos et al or Johansen et al, each in view of Maurer et al as applied to claims 9-11 above, and further in view of Serban et al (US Patent No. 4,782,014) for reasons of record in paper no. 5 and is reiterated herein below.

Examiner thanks the Applicant for pointing out an error in the statement of rejection. The Examiner did misstate the rejection and Serban et al is cited instead of Campbell.

See the discussions of Nyirkos et al, Johansen et al and Maurer et al above. These references differ from the instant invention in failing to specifically teach the provision of polyclonal or monoclonal antibodies to YKL-40 and appropriate reagents in kits.

Serban et al teach a new method of immunological analysis for serum amyloid A protein (SAA) and serum amyloid P-component (SAP), kits and a method of purification of SAA and SAP. Serban et al teach that changes in concentration and ratio of acute phase proteins, e.g. CRP

and SAA, and of SAP are important for diagnosis and management purposes of a number of acute and chronic inflammatory diseases such as rheumatic conditions, e.g. rheumatoid arthritis, juvenile polyarthritis, ankylosing spondylitis, Reiter's syndrome, psoriatic arthritis or rheumatic fever, vasculitis syndromes, Chron's disease, autoimmune conditions, e.g. systemic lupus erythematosus or polymyositis, malignancies, transplant rejection and the like. Serban et al teach test kits containing, for example, a suitable carrier, e.g. a carrier having a plastic surface or a carrier coated with a polypeptide, polysaccharide or synthetic organic polymer bearing nitrophenyl groups, preferably trinitrophenyl groups, optionally solutions of a compound bearing nitrophenyl groups, preferably trinitrophenyl groups, solutions of a monoclonal or of polyclonal antibodies binding SAA or SAP, and, if said first antibodies are not labeled with an enzyme, solutions of polyclonal, enzyme-conjugated second antibodies binding said first antibodies, enzyme substrates in solid or dissolved form, standard solutions of SAA and/or SAP, buffer solutions and optionally calcium salts or related bivalent salts such as zinc or cupric salts in solid or dissolved form, and optionally pipettes, reaction vessels, calibration curves, color intensity tables and the like. The solutions may be in concentrated form or freeze-dried requiring dilution with water or buffer solution before use. See column 4, line 37 through column 5, line 3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the various reagents taught by Nyirkos et al, Johansen et al and Maurer et al in a kit because the use of kits has the advantages of easy storage, economy and convenience such as taught by Serban et al. A skilled artisan would have had a reasonable expectation of success in assembling various reagents into kits because Serban et al teach that such kits can incorporate many different reagents and apparatus appropriate for performing an immunoassay, and that such kits are routine used in the art to detect various conditions including acute and chronic inflammatory diseases such as rheumatic conditions.

***Response to Arguments***

**9.** Applicant's arguments filed 8/8/00 have been fully considered but they are not persuasive.

Applicant argues that the references do not make obvious the claims inventions of claims 9-11 because Nyirkos et al and Johansen et al fail to describe a relationship between YKL-40 level and cirrhosis of the liver. Applicant argues that a prima facie case of obviousness requires that the combination of the cited art must provide all of the elements of the claimed invention. In addition, there must be some teaching, suggestion, or motivation to combine the references, and to support an obviousness rejection, the cited references must provide a reasonable expectation of success. These arguments have been fully considered but are not deemed to be persuasive. The references have been explained as to their relevance and the statement of motivation has been provided in the previous office action and in the instant office action. Furthermore, the rejected claims are directed to an antibody to YKL-40 and do not require a relationship between YKL-40 and cirrhosis of the liver. Although Nyirkos et al, Johansen et al and Maurer et al do not specifically teach antibodies to YKL-40, the combination of these references makes obvious the fact that antibodies to YKL-40 can be produced and used in an assay to detect YKL-40. Both Nyirkos et al and Johansen et la teach the need for detection and quantitation of the molecule and Johansen et al specifically teach that immunoassay is one of two means by which proteins produced by different cell types can be identified, and Maurer et al teach that antibodies, both polyclonal and monoclonal, can be produced against virtually any macromolecule, providing one of ordinary skill in the art a high expectation of success in raising the necessary antibodies and motivation for the use of the antibodies in an assay.

Applicant argues that the cited art, individually or in combination, fails to teach or suggest a relationship between YKL-40 level and cirrhosis of the liver and thus fails to teach or suggest all the limitation of the instant claims.

This argument has been fully considered but is not deemed to be persuasive because the rejected claims are directed to antibodies to YKL-40 and kits comprising the same. The claims do not recite a relationship betweenYKL-40 and cirrhosis of the liver.

Applicant argues that the cited art fails to teach a viable assay because in vitro conditions are not predictive of in vivo cellular behavior. This argument has been fully considered but is not deemed to be persuasive because the rejected claims are directed to antibodies to YKL-40 and kits comprising the same. The claims do not recite an assay nor any in vitro conditions.

Applicant argues that without appropriate, normal in vivo controls, culture data does not indicate that a maker can distinguish between a pathological and a healthy state, and that lacking the proper statistical analysis, in vitro data fails to establish that a marker can distinguish between healthy and pathological states. This argument has been fully considered but is not deemed to be persuasive because the rejected claims are directed to antibodies to YKL-40 and kits comprising the same. The claims do not recite the ability of a marker to distinguish between a pathological and a healthy state.

### *Allowable Subject Matter*

**10.** The following is a statement of reasons for the indication of allowable subject matter:

Claims 1-8 are allowable. The claims are allowable because the prior art of record fail to teach a method of screening for a disease state in a patient population suspected of having cirrhosis of the liver, said method comprising measuring the level of YKL-40 in a biological sample of the patient and comparing the level to that of normal, healthy individual, wherein a statistically significant difference indicates the presence of said disease state.

### *Conclusion*

**11.** **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

**12.** Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy Nguyen whose telephone number is (703) 308-4243. The examiner can usually be reached Monday through Wednesday, from 8:30 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399. The fax phone number for this Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bao-Thuy Nguyen
Patent Examiner
Art Unit 1641
November 15, 2000

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641